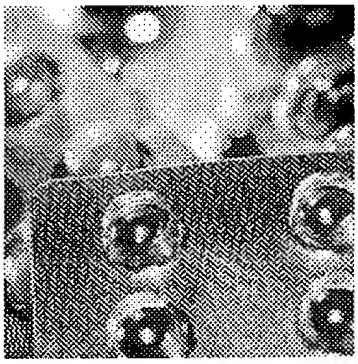
Pharmaceutical Blister Packaging, Part II

Machinery and Assembly

Ron Pilchik



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Blister packaging and labeling is quickly being recognized as a beneficial tool in helping manufacturers protect and promote their products and meet new regulations. Part II of this article reviews **the machinery, assembly, and costs of blister packaging** and discusses how clinical trials and recent regulatory developments will grow the blister packaging industry in the United States.

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Blister packs are portable, can help patients follow drug regimens, and can protect drugs over a long shelf life. Advocates cite several aspects in which blister packaging is better than conventional packaging, including product integrity, product production, tamper evidence, reduced possibility of accidental misuse, and patient compliance. Part I of this article discussed the materials used for blister packages and typical blister constructions (1). Part II reviews the machinery, assembly, and costs of blister packaging and discusses future trends.

Blister packaging machinery

Modern thermoform–fill–seal machines can operate at speeds ≤800 packages/min. Today, much of the emphasis in improving production is placed on applying microprocessor controls that electronically connect the filling and forming equipment with other downstream machinery for cartoning and wrapping. These controls also feed tablets or liquids into the unit-dose blisters, ensuring that an exact volume is put into each. Modern machinery also uses integrated vision systems to help ensure the accuracy of the fill and the integrity of the product in the blister. These machines have become quite versatile and can readily accommodate several types of lidstocks and basestocks, allowing the manufacturer to obtain better compatibility between the medicine and its packaging material as well as better patient compliance.

Blister packaging offers many advantages to the industry and to the public, and the machinery will continue to support this proven form of pharmaceutical packaging. Improvements in the form, materials, and machinery for blister packaging will continue to increase the applicability of this method for containing and distributing pharmaceutical products. Figure 1 shows an example of a blister packaging machine.

General assembly. The sequence involves heating the plastic, thermoforming it into blister cavities, loading the blister with the product, placing lidding material over the blister, and heat-sealing the package. This can be a simple manual process, or it can be partially or fully automated. Although purchasing empty, preformed blisters and lidding material and then filling the product in a separate step is possible, this is rarely done. Instead, the package is created and filled on the same machine (see Figure 2).

Detailed assembly. Blister packaging machines typically operate with intermittent motion. The seal is made during the dwell time required for thermoforming. The essential parts and functions of an intermittently operating packaging machine include the following.

The unwinding station. The unwinding station supplies the forming films and the lidding material at a rate corresponding to the speed of the packaging machine (see Figure 1, part A).

The heating station. The heating station raises the temperature of the plastic forming films to a level suitable for deep drawing. Forming films containing the polyvinyl chloride (PVC) support material are heated to 120–140 °C. Polypropylene (PP) forming films are heated to 140–150 °C. Forming films containing aluminum are not heated before the forming process (see Figure 1, part B).

The forming station. The forming station forms the plastic blister cavities via compressed air or die plates. Films containing

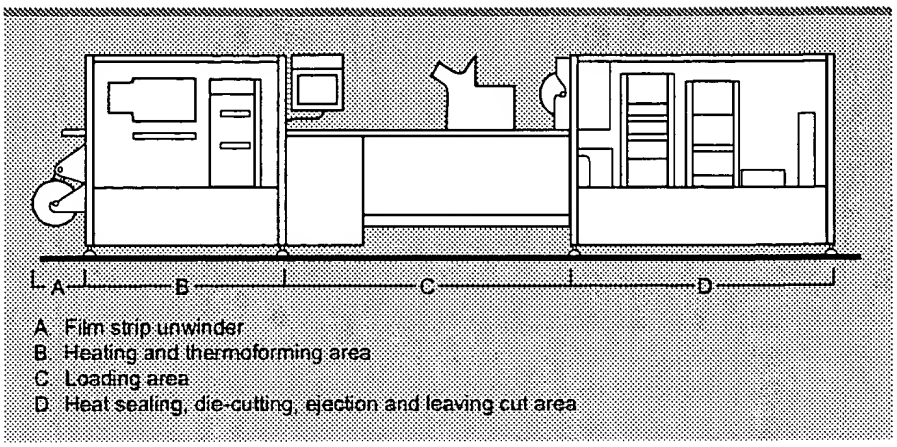

Figure 1: A blister packaging machine.

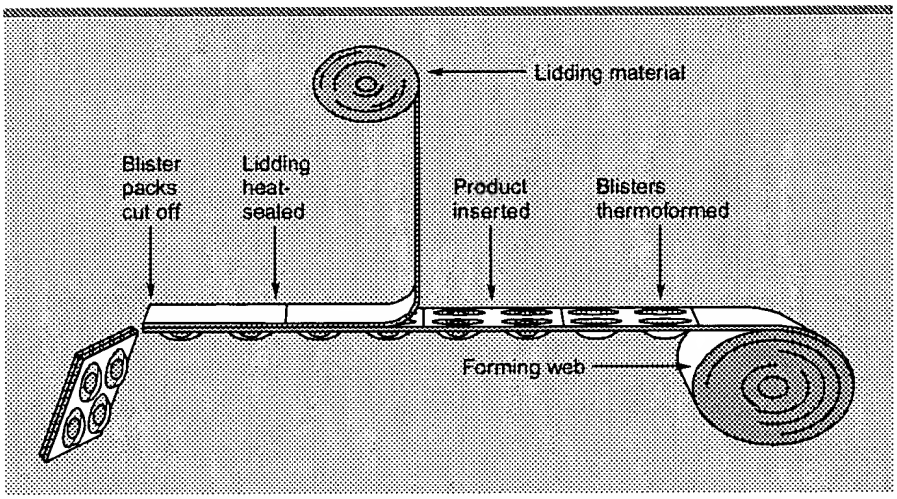

Figure 2: A typical procedure for blister packaging assembly.

Table I: Representative cost comparisons for packages containing 30 tablets

Packaging Material	Material Costs ($)	Labor Costs ($)	Total Costs ($)
Glass bottle	0.51	0.70	1.21
Plastic bottle	0.125	0.70	0.825
Blister pack	0.07	0.25	0.32

aluminum are formed with mechanical forming tools only (see Figure 1, part B).

The cooling station. The cooling station cools PP films after the forming process. Laminates containing PVC or aluminum do not need to be cooled.

The feeding machine. The loading area fills the blister cavities with product. The feeding machine can be linked, or the product to be packaged can simply be swept into the blisters (see Figure 1, part C).

The sealing station. The sealing station heat-seals the lidding material to the forming film that contains the product (see Figure 1, part D). All heat-sealing methods mate the blister and lid under constant pressure for a specified time, during which heat is supplied. The mating surfaces fuse and bond, setting almost instantaneously when heat input stops. Depending on the type of machine, the sealing temperature typically ranges between 140 and 340 °C.

The cooling station. The cooling station is necessary with all forming films (see Figure 1, part D). PP forming films must be cooled longer than other types of film.

Labeling through packaging. Packages are labeled, notched, and then marked with a batch number at the coding station. The perforating device makes a cross-shaped perforation along the sealing seams. At the punching station, the packages are then separated into sheets that typically contain from 10 to 20 individual blisters.

The vision system checks the filled packages for defects. Finally, a multipacking machine packs the individual packages into bigger cartons.

Blister packaging costs

The package can significantly affect the profitability of drug products. Packaging costs are ~10% of the total product cost for ethicals and as high as 50% of the total cost for over-the-counter (OTC) products. Therefore, sales can be positively or negatively influenced by the package, especially in the case of OTC products.

Cost comparisons. The costs of various drug packages rarely are published. However, one cost study reported that blister packaging for unit-dose oral medications is cost-competitive with bulk packaging in bottles (3). The study compared 60- and 125-cm^3 bottles with five sizes of blisters, dosage counts from 7 to 100, and six blister structures (PVC, PVDC-coated PVC, and PVC/Aclar [Honeywell, Morristown, NJ] in child-resistant and non-child-resistant versions). The researchers also considered expenses incurred for each component, including

- packaging-line operation (e.g., machinery, line speed, efficiency, and staffing)
- shipping
- freight
- distribution
- pharmacy inventory and dispensing.

The study found that when total system costs (including repackaging supplies and pharmacists' time) are considered, blister packaging can represent a significant savings over conventional bottles. For example, a child-resistant, PVC blister package can save as much as $4.58 per 100 doses when compared with a bottle. From a manufacturing perspective, however, bottles tend to be more economical than blister packages except for the most compact blister formats and the simplest structures. Table I lists cost comparisons from the study.

In this example, even if material costs were doubled, a blister design would still be favorable because the blister component accounts for only part of the material cost, with the rest being the lidding structure, and the total cost would be just

$0.32 per package. The fact that labor savings account for most of the advantage in the cost of blisters over plastic or glass bottles is typical of flexible packaging because of its higher degree of automation. In addition, economies of production are better in blister packaging because it is fully automatic and requires minimum human support.

Break-even point. At some product-quantity point, the blister packaging loses its advantage, and bottles become more cost-effective than blister packs. Generally speaking, that break-even point is the 100-count unit. Tablets distributed in quantities of <100 can be packaged most economically in blisters — say, 10 cards of 10 tablets each. Pharmaceutical products distributed in quantities higher than that can be packaged most economically in bottles. Therefore, this study indicated that blister packaging is cheaper for small package counts in the 50–100 range and more expensive for package counts >100.

Future trends in blister packaging

Unit-dose packaging is a major trend with a strong influence on blister packaging. In addition, two major forces will have an enormous effect on the growth of blister packaging in the United States: clinical trials and regulatory developments.

Clinical trials. With the increasing incidence of clinical trials, many of which require complex regimens, more pharmaceutical companies are using blister packaging. From a convenience and patient compliance standpoint, the use of blister packaging in clinical trials can be beneficial. For example, for a dose-range study in which patients should take four tablets (or placebo) per day, the easiest packaging method is a blister pack. It is less convenient for a patient to take a tablet from one bottle, then a tablet from another bottle, etc. With a blister pack, all the medication is in one place and is easily marked.

New regulations. Two regulatory developments relating to iron supplements and methamphetamine manufacturing also will affect the future growth of blister packaging.

Iron supplements. FDA's final rule titled "Iron-Containing Supplements and Drugs: Label Warning Statements and Unit-Dose Packaging Requirements" took effect on 15 July 1997 (2). One provision of the ruling calls for unit-dose packaging for iron-containing products containing at least 30 mg of iron per dosage unit. Some companies have had to take iron products off the market because they were not in unit-dose packaging. Thus, to be in compliance, these companies will have to use blister packaging.

Methamphetamine manufacturing. On 3 October 1996, President Clinton signed into law the comprehensive Methamphetamine Control Act of 1996. The law broadens control over certain chemicals used in the production of methamphetamines, increases penalties for the trafficking and manufacture of methamphetamines and listed chemicals, and expands regulatory controls to include the distribution of certain lawfully marketed products that incorporate ephedrine, pseudoephedrine (PSE), and phenylpropanolamine (PPA). The law subjects transactions involving PSE and PPA to the registration, record-keeping, and reporting requirements of the Controlled Substances Act.

However, the law creates a safe-harbor exemption for the retail sale of ordinary OTC products that contain PSE and PPA. To be included in the safe harbor, the product must meet the following two requirements:

- The package must contain not more than 3 g of the base ingredient.
- The product must be in blister packs of not more than two tablets per blister (unless use of a blister pack is technically impossible, such as for liquids).

For products not packaged in accordance with the safe-harbor exemption as of 3 October 1997, pharmaceutical retailers are required to register with the Drug Enforcement Administration if they sell more than 24 g in a single transaction and to keep records of such transactions. In other words, to avoid the paperwork involved in registering, a retailer should sell certain OTC products containing PSE and PPA in blister packaging. The law is designed to stop the unscrupulous manufacture of illegal drugs from these substances by making it more difficult to open each blister package to acquire the required amount of drug.

Conclusion

Demand for pharmaceutical packaging is increasing and will continue to do so as companies in the highly competitive and rapidly changing pharmaceutical market come to rely more on packaging to protect and promote their products. Although healthcare practitioners usually select the pharmaceutical product, drug manufacturers must design their packaging with users in mind. Just as appearance and ease of use are important for consumer products, they are key to a drug's success. Furthermore, for those OTC drugs and nutritional supplements, consumer appeal is paramount.

Companies that use blister packaging will definitely have to face both challenges and opportunities. Packaging engineers have been called upon to develop creative solutions for meeting the Consumer Product Safety Commission's child-resistant and senior-friendly requirements. With additional regulatory developments such as the International Conference of Harmonization's testing guidelines and FDA's rule on iron supplements, a large increase in blister packaging use, along with the use of innovative materials and designs, is expected. **PT**

Reference

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2. *Code of Federal Regulations, Title 21, Food and Drugs*, Parts 101, 111, and 310 (January 1997).
3. Michigan State University School of Packaging (East Lansing, MI, 1994).